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Review

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Symptomatic and quality-of-life outcomes after treatment for clinically localised prostate cancer: a systematic review

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To conduct a systematic review of the risks of short-term outcomes after major treatments for clinically localised prostate cancer. MEDLINE, EMBASE and the Cochrane Library were searched from 2004 to January 2013. Study arms that included ≥100 men with localised prostate cancer in receipt of surgery, radiotherapy or active surveillance and reported symptomatic and quality-of-life (QoL) data from 6 to 60 months after treatment were eligible. Data were extracted by one reviewer and checked by another. In all, 64 studies (80 treatment cohorts) were included. Most were single treatment cohorts from the USA or Europe. Radiotherapy was the most common treatment (40 cohorts, including 31 brachytherapy cohorts) followed by prostatectomy (39 cohorts), with only one active surveillance cohort. Most frequently measured symptoms were urinary, followed by sexual, and bowel; QoL was assessed in only 17 cohorts. Most studies used validated measures, although poor data reporting and differences between studies meant that it was not possible to pool data. Data on the precise impact of short-term symptomatic and QoL outcomes after treatment for localised prostate cancer are of insufficient quality for clear guidance to men about the risks to these aspects of their lives. It is important that future studies focus on collecting core outcomes through validated measures and comply with reporting guidelines, so that clear and accurate information can be derived for men considering screening or treatment for prostate cancer.

Keywords

prostate cancer, systematic review, patient-reported outcome measures

Introduction

Screening for prostate cancer remains controversial because testing for PSA leads to the diagnosis of large numbers of tumours that may not become life-threatening or clinically apparent during a man's lifetime. Current management options for clinically localised prostate cancer include radical surgery and radiotherapy (RT) treatments with curative intent, which risk damage to urinary, bowel, and sexual functioning, or active monitoring or surveillance that aim to avoid radical treatment and its consequences in the short-term, but may miss the opportunity for cure. Randomised controlled trials (RCTs) of screening [1,2] and treatment [3,4] have focused their major reports on rates of mortality and the incidence of metastases and clinical disease progression, with relatively little attention devoted to symptomatic and quality-of-life (QoL) impacts.

Many observational studies have provided data attempting to specify and quantify symptomatic and QoL outcomes. Systematic reviews published in 2008 and 2011 included all outcomes, but, as with the major RCTs, focused particularly on clinical outcomes [5,6]. The reviews of symptomatic and QoL outcomes concluded that all treatments – including androgen-deprivation therapy (ADT), radical prostatectomy (RP) and RT – caused urinary, bowel, or sexual dysfunction [5,6]. The 2008 review added that studies did not report consistent definitions for outcomes, or report similar follow-up periods, and that they varied in whether baseline rates were assessed, and what measures were used [5]. In the 2011 review, particular studies were identified that showed that RP resulted in higher levels of erectile dysfunction and urinary incontinence than RT, and that RT was also associated with bowel dysfunction [6]. Both reviews noted that symptomatic and QoL data were variably assessed and that detailed conclusions were difficult because of limitations in the evidence [5,6].

A more recent review was undertaken of the use of validated patient-reported outcome measures (PROMs) in large

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prospective studies, with the aim of developing a core outcome set [7]. This found that the studies were difficult to interpret because of poor reporting and patient selection related to cohort design, but recommended that five domains should be studied for assessment of treatments for localised disease: urinary incontinence, urinary obstruction and irritation, bowel-related symptoms, sexual dysfunction, and hormonal symptoms [7].

Since these reviews were undertaken, there has been increasing attention to the importance of collecting patient-reported symptomatic and QoL data, particularly through standardised and validated PROMs [8]. In addition, new treatment modalities, such as laparoscopic and robotic surgery, brachytherapy (BT) and active surveillance/monitoring, have become more widespread, mostly with the aim of improving patient outcomes by reducing short-term symptomatic side-effects.

We undertook a systematic review of the published literature focusing on the assessment of symptomatic and QoL outcomes, including methods of measurement as well as the use of validated PROMs. The aim was to build on the previous reviews to provide clarity about the risks of short-term (6–60 months) outcomes after the major treatments for clinically localised, PSA-detected prostate cancer, and, where possible, to pool data from PROMs using meta-analysis.

Methods

This review followed guidance published by the Centre for Reviews and Dissemination and the Cochrane Collaboration [9,10]. We established a protocol for the review (available from the authors on request).

Data sources and searches

The previous review by Wilt et al. 2008 [5], evaluated studies published up to 2004; this review therefore only considered the literature published subsequently. Studies were identified by searching MEDLINE, the Excerpta Medica database (EMBASE) and The Cochrane Library [Cochrane Database of Systematic Reviews, the Cochrane Central Register of Controlled Trials, Database of Abstracts of Reviews of Effects (DARE) and Health Technology Assessment (HTA) databases)], all from 2004 to January 2013. We combined text word and Medical Subject Headings (MeSH) search terms for prostate cancer, the treatments and outcomes of interest (Appendix S1). We excluded studies published in languages other than English, letters or commentaries. Search results and full text articles were independently assessed for inclusion by two reviewers; disagreements were resolved through consensus or referral to a third reviewer. The intention was to update searches for outcomes for which sufficient data were available to permit meta-analysis.

Study selection

Study arms that included ≥100 men with clinically diagnosed localised prostate cancer and prospectively collected symptomatic and QoL outcome data (6–60 months) were eligible. We included studies of men with clinically localised prostate cancer – TNM stage T1 or T2 [11] in ≥95% of participants. We included cohorts with the following treatments: RP (robot-assisted, laparoscopic or open), RT (including external-beam RT (EBRT) and BT], active surveillance or watchful waiting. ADT was allowed in combination with other treatments as adjuvant or neoadjuvant therapy. We defined short-term outcomes as those occurring between 6 and 60 months after primary treatment for prostate cancer. Short-term symptomatic and QoL outcomes included those relating to urinary, bowel, hormonal or sexual function or bother, mood, general QoL, or generic health status.

We excluded studies involving only a single surgeon or the first cases of a new surgical treatment in a hospital (so called 'learning curve' studies). Studies were also excluded if men received a combination of treatments, if there was insufficient information to categorise the prostate cancer stage, when it was not possible to extract outcome data separately for different treatments, or if studies did not report baseline values for the outcomes of interest.

Data extraction and quality assessment

Data extraction was performed by one reviewer and checked by a second; disagreements were resolved through consensus or referral to the review team. We extracted data on: study design, year, country, number of centres, participant characteristics, type of treatment, duration of follow-up, PROM used or other measure, and the short-term symptomatic and QoL outcomes measured. All included studies were single or multiple treatment cohorts or were analysed as such and so were considered at high risk of bias. A formal quality assessment was therefore not conducted.

Data synthesis and analysis

We grouped outcomes into the following domains: urinary, sexual, bowel, hormonal, anxiety, depression, coping, QoL, and 'other'. We summarised the number of treatment cohorts that reported each different outcome within these domains, separately for each of the different treatments. For outcomes reported by four or more treatment cohorts we investigated whether it was possible to conduct further analyses for these outcomes. If further analysis was possible, we intended to estimate summary mean differences and relative risks together with 95% CIs using random-effects models. Where meta-analysis was not possible, we summarised the reasons for this. For the most commonly evaluated symptoms (sexual potency and urinary continence), we reported the range in

the proportion of patients who reported these symptoms at 6, 12 and 24 months of follow-up stratified according to treatment.

Results

The searches identified 12 355 references from 2004 to 2013 of which 726 were considered potentially relevant based on title and abstract screening. In all, 64 studies evaluating 80 treatment cohorts were included: two RCTs [12,13], nine multiple treatment cohorts [14–22], and 53 single treatment cohorts [23–75] (Fig. 1). The two RCTs compared different forms of the same treatment (BT [12] and EBRT [13]). In all, 35 studies were from the USA, 21 from Europe, five from Canada, four from Asia, two from Australia, one from Israel, and two were multi country (one from the USA and Spain and one from the USA and Canada). RP was the most commonly evaluated treatment: 24 cohorts assessed open RP, 10 assessed laparoscopic RP, four assessed robot-assisted RP, and one assessed mixed open RP and robot-assisted/laparoscopic RP. BT was assessed in 31 cohorts, RT (including EBRT, conformal and stereotactic body RT) in nine cohorts. Only one cohort assessed active monitoring [60]. Where reported, the age range was 36–91 years across studies, the median age range was 56–60 years and the mean age range was 57–70 years. Details of included studies are provided in Appendix S2 [12–75].

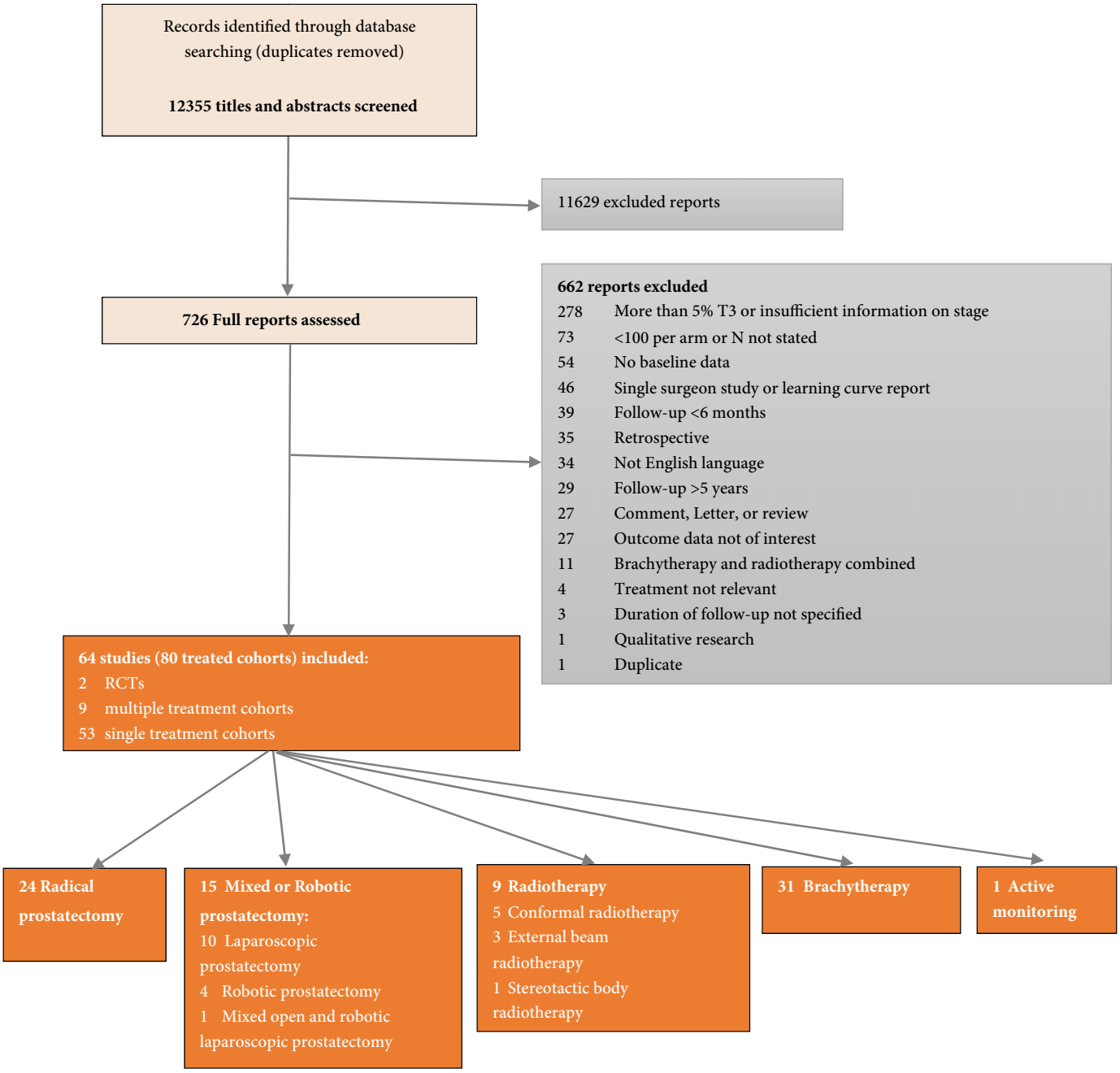
The most frequently reported outcomes were urinary symptoms: 55 of the 64 studies (67/80 cohorts) reported some measure of urinary function (Table 1) [29,81–96]. Of these, 49 studies measured urinary symptoms using a validated PROM, including the IPSS (22 cohorts), Expanded Prostate cancer Index Composite (EPIC; 15 cohorts), AUA Symptom Index (AUASI; 14 cohorts), and the University of California, Los Angeles Prostate Cancer Index (UCLA PCI; 13 cohorts). Other validated scales such as the European Organisation for Research and Treatment of Cancer quality of life questionnaire prostate specific 25-item (EORTC QLQ-PR25) and the International Continence Society (ICS)Male questionnaire were reported in less than five cohorts. Sexual symptoms were also reported by most studies, with 43 studies (55 cohorts) reporting some measure of sexual function, 36 using validated PROMs. Most studies reported sexual function using validated PROMs such as the EPIC (16 cohorts), UCLA PCI (12 cohorts), or International Index of Erectile Function (IIEF; 10 cohorts). Various non-validated measures were also used to assess urinary and sexual outcomes. Bowel and hormonal symptoms were less commonly reported with only 14 studies (18 cohorts) reporting some measure of bowel functioning and six studies (10 cohorts) reporting hormonal function, all using validated PROMs (EPIC and EORTC QLQ-PR25). Of the studies that reported bowel function, 10 assessed EBRT or BT, and eight RP, meaning that nine of the RT cohorts did not report any measure of bowel function. QoL was reported in 12 studies (17 cohorts), most commonly using a variation of the 36-item short-form health survey (SF-36; 12 cohorts), the EORTC QLQ-30-item core (C30; five cohorts) or the Functional Assessment of Cancer Therapy – General (FACT-G) and FACT – Prostate (FACT-P, three cohorts). Other measures such as anxiety [Memorial Anxiety Scale for Prostate Cancer (MAX-PC) and State-Trait Anxiety Inventory six-item (STAI-6)], depression [Center for Epidemiologic Studies Depression scale (CES-D)], and coping (Utrecht Coping List) were each reported in two or fewer cohorts.

Studies often reported on multiple outcomes, appropriately using different dimensions of the same scale such as the EPIC, UCLA PCI or EORTC QLQ. Thirteen studies used the EPIC, and of those four provided data for all four components of the measure (urinary, bowel, hormone, sexual symptoms), three provided data for three components (urinary, bowel, sexual symptoms), two provided data for two components (urinary and bowel or urinary and sexual symptoms), and four assessed single components of the tool (urinary in one, sexual in three). Eleven studies used the UCLA PCI, and two assessed all three components (urinary, bowel, sexual), six assessed two components, and three assessed single components. Five studies assessed the EORTC, but none assessed all five components (urinary, bowel, sexual, hormone, QoL); three assessed four components and two assessed single components (hormonal or QoL).

We investigated whether studies had reported outcome data sufficiently consistently to permit pooling. For pooling to be possible we specified that a minimum of four treatment cohorts were required to report a single outcome for a specified treatment. We found that it was not possible to pool data for any outcome for any treatment. Reasons why pooling was not possible included presentation of a mixture of continuous and dichotomous outcomes, lack of reporting of SD or other measure of variance for continuous outcome, reporting of outcomes after different periods of follow-up, assessing different components/versions of a measure, only reporting data graphically or reporting different measures on graphs, and using different thresholds to dichotomise results. Data suitable for pooling for any single outcome were provided only by two cohorts at most. Table 2 [81–84,86] provides an overview of reasons why pooling was not possible for each outcome, stratified according to treatment.

As data were not appropriate for pooling, we summarised the range of incidence of urinary and sexual symptoms at 6, 12 and 24 months of follow-up, stratified according to treatment (Table 3). It was not possible to provide this information for other outcomes such as bowel or QoL outcomes, as dichotomous data were not provided by a sufficient number of studies. Most studies that dichotomised data on urinary symptoms provided data that allowed us to calculate the proportion of continent patients, although the exact way in

Fig. 1 Flow of reports through the review process.



which this was defined varied considerably across studies, as did the way in which it was assessed, so detailed conclusions could not be easily drawn.

In general terms, there were a larger proportion of continent patients in the BT- and EBRT-treated cohorts compared with the RP-treated cohorts, although the number of continent patients tended to improve with time for all treatment groups. There was no difference between open and laparoscopic/robot-assisted RP until 24 months, when the number of continent patients was greater with laparoscopic/robot-assisted RP, although cohort numbers were small. Sexual symptoms were assessed as the number of potent men, although the exact definition of this also varied with the most common being 'erection sufficient for intercourse' or 'return to baseline sexual function'. Many studies restricted this analysis to patients with 'normal' sexual function at baseline. Differences between treatment groups were less clear for potency, although there was some suggestion that this was

Table 1 Number of treatment cohorts that reported each short-term outcome measure.

Domain	Outcome measure and reference to measure	Number of treatment cohorts					
		Total	RP	Laparoscopic or robot-assisted RP	RT	BT	Active monitoring
Urinary	AUASI [81]	14	4	1	2	7	
	IPSS [82]	22	1	3		18	
	EPIC: Urinary symptoms [83]	15	4	4	5	2	
	UCLA PCI: Urinary symptoms [84]	13	7	5		1	
	EORTC QLQ-PR25: Urinary symptoms [85]	4	1			3	
	ICSMale	3	2	1			
	Patient-completed, non-validated	3		2		1	
	Other, non-validated	8	4	2		2	
Sexual	EPIC: Sexual symptoms [83]	16	6	4	4	2	
	UCLA PCI: Sexual symptoms [84]	12	6	5		1	
	IIEF/IIEF-5 [86, 87]	10	5	2		3	
	EORTC QLQ-PR25: Sexual symptoms [85]	4	1			3	
	SAQ Q [88]	4	1		2	1	
	SHIM [89]	4	1	3			
	Patient-completed, non-validated	3	1			2	
	Other, non-validated	5	1	1		3	
Bowel	EPIC: Bowel symptoms [83]	13	4	2	5	2	
	EORTC QLQ-PR25: Bowel symptoms [85]	4	1			3	
	UCLA PCI: Bowel symptoms [84]	2	1	1			
	Non-validated: Bowel symptoms	1				1	
Hormonal	EPIC: Hormonal symptoms [83]	8	3		3	2	
	EORTC QLQ-PR25: Hormonal Treatment related symptoms [85]	2	1			1	
QoL	EORTC QLQ-C30 [90]	5	2			3	
	FACT-G [91]	3	1		1	1	
	FACT-P [92]	3	1		1	1	
	SF-36 various versions	12	6	1	1	4	
	QoL not specified	1		1			
Anxiety	MAX-PC [93]	1					1
	STAI-6 [94]	1					1
Depression	CES-D [95]	2				1	1
Coping	Utrecht Coping List [96]	1				1	
Other	Symptoms and QoL [29]	1			1	1	
Total		**87**	**24**	**15**	**13**	**34**	**1**

AUASI, AUA Symptom Index; CES-D, Center for Epidemiologic Studies Depression; EORTC QLQ, European Organisation for Research and Treatment of Cancer quality of life questionnaire; EPIC, Expanded Prostate Cancer Index; FACT-G, Functional Assessment of Cancer Therapy – General; FACT-P, Functional Assessment of Cancer Therapy – Prostate; ICS, International Continence Society Male Questionnaire; IIEF, International Index of Erectile Function; MAX-PC, Memorial Anxiety Scale for Prostate Cancer; SAQ Q, Sexual Adjustment Questionnaire; SF-36, 36-item short-form health survey; SHIM, Sexual Health Inventory for Men; STAI-6, State Trait Anxiety Inventory six-item; UCLA PCI, University of California, Los Angeles Prostate Cancer Index.

lower with RP than EBRT and BT. As with continence, potency improved a little after RP. It remained similar over time after EBRT and BT. However, it should be noted that no formal statistical comparisons between treatment groups was possible due to the differences in the way that symptoms were measured between studies. Any comparisons are also based on evaluations within single treatment cohorts rather than within study comparisons.

Discussion

The present review identified 64 studies evaluating short-term symptomatic and QoL outcomes in 80 cohorts assessing RP (39 cohorts), RT (40 cohorts) or active surveillance (one cohort) for localised prostate cancer. Most studies were single treatment cohorts (53 studies) and most were undertaken in the USA (40) or Europe (21). Patients involved in these studies were mostly aged 56–70 years, which is the age-group suitable for these radical interventions. However, the ages actually ranged from 36 to 91 years, which suggests that some studies included patients who might not be able to benefit from treatment. The most commonly assessed symptomatic outcomes were related to the urinary tract, with 55 studies reporting at least one measure of urinary function, 49 of which used a validated PROM to assess some aspect of urinary function. Sexual function symptoms were assessed in 43 studies, with validated PROMs used in 36 (the EPIC in 16 cohorts, the UCLA-PCI in 12, and the IIEF in nine). Bowel symptoms were assessed mostly through the EPIC (13 cohorts), with the EORTC QLQ (four) and the UCLA PCI (two). QoL was assessed in only 12 studies in total, with 10 cohorts using a version of the SF-36, five the EORTC QLQ and three the FACT-G and FACT-P. Other outcomes such as

Table 2 Reasons why meta-analysis was not possible for each outcome stratified according to treatment.

Domain	Outcome measure and reference to measure	Treatment	Number of cohorts	Meta-analysis possible	Reason
Urinary	AUASI [81]	RP	4	No	No SD or measure of variance: 1 cohort Follow-up time varied between studies: 12 months in 2 cohorts, 6 months in 2 cohorts. Different component of AUASI reported: AUA-7 symptom index (1 cohort), AUSASI obstruction (1 cohort), AUA symptom score (1 cohort), urinary bother, dysfunction and limitation(1 cohort)
		BT	7	No	No SD or other measure of variance: 3 cohorts 3 components of the score not overall AUASI score: 1 cohort Mean and SD overall AUASI score at baseline, 6 and 12 months: 3 cohorts
	IPSS [82]	BT	18	No	Only reported data graphically: 10 cohorts; of these only 2 reported means and SDs, others reported data as medians with IQR and range or means and medians alone. Dichotomised data using different thresholds: 3 cohorts Continuous data (medians or means) with no measure of variation: 5 cohorts
	EPIC: Urinary symptoms [83]	RP	4	No	Dichotomous data: 1 cohort Continuous data: 4 cohorts No SD or measure of variance: 1 cohort Urinary summary score at 6 and 12 months: 2 cohorts Urinary function irritation/obstruction: 2 cohorts (1 graph only), 1 using EPIC-26, 1 EPIC version not reported Urinary function/incontinence: 2 cohorts (1 graph only), 1 using EPIC-26, 1 EPIC version not reported
		Laparoscopic or robot-assisted RP	4	No	Continuous data: 2 cohorts Subgroup data only, no overall data: 1 cohort Both reported data at 12 months based on the same EPIC subscales Dichotomous data: 2 cohorts Both reported number with no pads at 6 and12 months, other outcomes varied
		RT	5	No	Continuous data: 5 cohorts Data only available graphically: 3 cohorts No SD or measure of variance: 1 cohort Dichotomous data: 1 cohort
	UCLA PCI: Urinary symptoms [84]	RP	7	No	No SD or measure of variance: 1 cohort Mean, SD at 6 and 12 months for urinary function: 2 cohorts Dichotomous/categorical data using different thresholds: 4 cohorts Data reported for different time points: 24 month (2 cohorts), 12 months (1 cohort), 6 months (1 cohort), 48 months (1 cohort)
		Laparoscopic or robot-assisted RP	5	No	Dichotomised data using different thresholds: 4 cohorts Continuous data: 1 cohort
Sexual	EPIC: Sexual symptoms [83]	RP	6	No	Dichotomous data: 2 cohorts, 1 used EPIC-26 and 1 used EPIC-50 Continuous data: 5 cohorts Different measures: EPIC sexual subscale, bother and function (3 cohorts) – reported at 6 and12 months in 2 cohorts, at a mean of 20.1 months in 1 cohort; EPIC-26 sexual score (1 cohort), EPIC sexual score stratified by nerve-sparing subgroups only (1 cohort)
		Laparoscopic or robot-assisted RP	4	No	Dichotomous data: 3 cohorts Different subscales 2 cohorts reported dichotomous data for potency (number potent); 2 reported return to baseline for sexual function and sexual bother Continuous data: 2 cohorts Both reported data on sexual bother at 12 months
		RT	4	No	Continuous data: 3 cohorts Data only available graphically: 1 cohort No SD or measure of variance: 1 cohort Dichotomous data: 1 cohort
	UCLA PCI: Sexual symptoms [84]	RP	6	No	Continuous data: 2 cohorts Data for subgroups only: 1 cohort No SD or measure of variance: 1 cohort Dichotomous data: 4 cohorts Return to baseline sexual function: 3 cohorts, different follow-up times (6 months, 12 months, up to 12 months) Improvement in erectile function: 1 cohort

Table 2 (continued)

Domain	Outcome measure and reference to measure	Treatment	Number of cohorts	Meta-analysis possible	Reason
		Laparoscopic or robot-assisted RP	5	No	Continuous data: 1 cohort Dichotomous data: 4 cohorts 3 cohorts provided data on numbers of patients with erection sufficient for intercourse at 6 months; 2 studies also provided data at 12 and 24 months 1 cohort used different thresholds
	IIEF [86]	RP	5	No	Dichotomous/categorical data: 5 cohorts Different thresholds: score >19 (1 cohort), ≥22 (1 cohort), ≥15 (1 cohort), 5 categories (1 cohort), response to question 5 potent or not (1 cohort), Continuous data: 1 cohort, median only
Bowel	EPIC: Bowel symptoms [83]	RP	4	No	Dichotomous data: 1 cohort Continuous data: 3 cohorts No SD or measure of variance: 2 cohorts
		RT	5	No	Continuous data: 4 cohorts Data only available graphically: 2 cohort No SD or measure of variance: 1 cohort Dichotomous data: 1 cohort
QoL	SF-36	RP	6	No	Dichotomous data: 1 cohort Continuous data: 5 cohorts No SD or measure of variance: 2 cohorts Different version of tool (RAND vs SF-36): 1 cohort 2 cohorts provided data on SF-36 at 6 and 12 months of follow-up

AUASI, American Urological Association Symptom Index; EPIC, Expanded Prostate cancer Index Composite; IIEF, International Index of Erectile Function; SF-36, 36-item short-form health survey; UCLA PCI, University of California, Los Angeles Prostate Cancer Index.

depression, anxiety, and coping were only assessed in one or two cohorts.

It was encouraging to see the marked increase in the use of validated PROMs since the review in 2004 [5], and in the domains recommended as core outcomes [7]. Although a relatively wide range of measures was used, the numbers of studies using the same measures in the major domains of interest suggested that meta-analysis should have been possible. But sufficient pooling could not be achieved for any outcome because of the poor quality of data collection and reporting. There were inconsistencies in the presentation of outcomes – particularly the thresholds and periods of follow-up; different versions or components of PROMs used or reported; and incomplete presentation of data to allow pooling. It was also the case that some studies reported non-validated measures of urinary (eight cohorts), sexual (five), and bowel (one) function. Similar criticisms were made of studies in previous reviews when fewer PROMs were reported [5–7]. It is particularly disappointing that the increased use of validated PROMs does not appear to have improved the quality of data reporting sufficiently to permit adequate pooling, or even clear qualitative comparison. This means that any comparisons made or conclusions reached are subject to considerable bias and uncertainty.

The lack of data relating to active surveillance/monitoring was confirmed by a review of QoL in this area, which showed a paucity of data [76]. A study published since we conducted the searches for our present review used EPIC and SF-12 data for USA men with low-risk prostate cancer undergoing active surveillance [77]; more such studies are required. Although there have been claims that robot-assisted or laparoscopic RP might have reduced impact on symptomatic outcomes, the overall summary of results in the present review did not show this, and this was further confirmed in a recent review of best practice in RP, which revealed that incontinence and erectile dysfunction remained significant factors [78], with urinary incontinence still an important issue 60 months after robot-assisted RP, and rates of sexual dysfunction remaining comparable to open RP [57].

The most commonly used PROMs across the various domains were the EPIC, EORTC QLQ and UCLA-PCI measures, which include urinary, sexual, and bowel symptom evaluation (the EPIC and EORTC QLQ also include a hormone domain). Other symptom-specific measures were used for assessing urinary function (IPSS, AUASI, ICSMale) or sexual function (IIEF). Generic QoL was most commonly assessed by the SF-36, FACT or EORTC QLQ. The major domains suggested as core outcomes for localised disease are clear: urinary incontinence, urinary obstruction and irritation, bowel-related symptoms, sexual dysfunction, and hormonal symptoms [7]. It is now essential that future studies focus on these core domains, use the same PROMs, and comply with recommended methods of presentation and reporting, in general terms [8] and according to the specific measures. This is supported by the recent International Consortium for Health Outcomes Measurement (ICHOM) [79] initiative,

Table 3 Ranges in rates of urinary and sexual symptoms at 6, 12 and 24 months of follow-up, stratified by treatment.

Symptom	Measures	Thresholds reported	Follow-up, months	Ranges in rates of urinary and sexual symptoms, % (*N*)				
				RP	Laparoscopic or robot-assisted RP	RT	BT	Active monitoring
Urinary symptoms	EPIC	Number continent	6	49–82	42–76	94	91–98	NA
	UCLA PCI	No use of pads		5 cohorts (1497)	7 cohorts (2480)	1 cohort (264)	3 cohorts (1026)	
	ICSMale	0–1 pads/24 h	12	52–94	52–92	97	89–98	NA
	IPSS	Return to baseline continence		9 cohorts (3632)	10 cohorts (5260)	1 cohort (258)	4 cohorts (1114)	
	Non-validated	Return to 75% of baseline	24	76–80	80–97	97	96–99	NA
		Continence (not defined)		2 cohorts (1129)	3 cohorts (1573)	1 cohort (178)	2 cohorts (847)	
Sexual symptoms	EPIC	Potency (erection sufficient for intercourse)	6	16–23	15–60	38	42	NA
	IIEF	Potency (not defined)		2 cohorts (650)	7 cohorts (2674)	1 cohort (264)	1 cohort (288)	
	UCLA PCI	Potency (no or mild erectile dysfunction)	12	19–76	19–79	26–36	46–86	NA
	SHIM	Potency (intercourse in previous month)		10 studies (2738)	12 studies (5708)	2 studies (816)	3 studies (406)	
	Non-validated	Return to baseline sexual function	24	36–54	27–91	34	44–83	NA
		Ability to get an erection (always, almost always)		2 studies (620)	4 studies (1815)	1 study (178)	2 studies (373)	
		IIEF ≥15						
		IIEF ≥17						

which recommended measurement of the EPIC-26 (26-item short form version) urinary incontinence, irritative/obstructive bowel, sexual, and hormonal domains, with two additional questions from the EORTC QLQ-PR25 scale for sexual symptoms and one from a validated scale on erectile dysfunction aids. We hope that consistent use of a core set of outcomes will allow future systematic reviews to estimate summary effect sizes.

The major RCTs of screening and treatment of localised prostate cancer are either now in longer follow-up periods [Scandinavian Prostate Cancer Group Trial Number 4 (SPCG-4) and European Randomised Study of Screening for Prostate Cancer (ERSPC)] or did not report detailed PROMs in previous publications [the Prostate, Lung, Colorectal, and Ovarian cancer screening trial (PLCO) and the Prostate cancer Intervention Versus Observation Trial (PIVOT)]. The Prostate testing for cancer and Treatment (ProtecT) trial, funded by the UK National Institute for Health Research (NIHR) comparing open RP, EBRT, and active monitoring is due to publish in 2016 with a wide range of PROMs [80].

The strengths of the present review lie in its Cochrane-guided protocol and methods. The inclusion criteria restricted the review to larger studies with data on symptomatic and QoL outcomes after the major treatment modalities, reported at baseline and up to 60 months after treatment. Data were extracted to permit meta-analysis, and although it was not possible to complete this, the data collection strategy enabled clear identification of the weaknesses of the studies' data collection and presentation practices. The limitations of the present review include that some important small studies may have been missed and that the primary aim, meta-analysis to permit clarity of presentation of findings, was not possible. A further limitation is that we did not conduct a formal risk of bias assessment of the included studies. However, most of the included studies were single treatment cohorts all which were considered at high risk of bias. For the purposes of the present review, the included RCTs were also considered as single treatment cohorts as they compared specific forms of the same treatment rather than comparing two different treatment categories (e.g. they compared two forms of BT rather than comparing BT with RP). The number of multiple treatment cohorts was too small to allow a formal comparison of treatments within a single study. Any comparisons between treatment modalities are therefore based on evaluations within single treatment cohorts rather than within study comparisons.

In conclusion, the present review found, as did previous reviews, that data collection and presentation of the impact of short-term symptomatic and QoL outcomes after treatment for localised prostate cancer are of insufficient quality to permit precise guidance to men about the risks to these aspects of their lives. Studies now tend to include validated PROMs to assess

these important aspects, but much greater attention needs to be paid to collecting, analysing, and reporting these data according to high quality standards so that they can be synthesised. As evidence continues to suggest that PSA testing leads to the identification of many tumours that may not need treatment, and that radical treatments have an impact on important areas of a man's life, clear and accurate data about PROMs becomes even more important for men considering whether to have a PSA test, or which treatment to have when diagnosed with localised prostate cancer.

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Contributions

Jenny L. Donovan conceived the idea for the review and sourced the funding for the research. Margaret Burke designed the search strategy and ran the searches. Theresa H.M. Moore, Catherine M. Jameson, Philippa Davies, Mari-Anne Rowlands and Rebecca Beynon selected studies for inclusion and undertook the data extraction. Jelena Savovic and Penny F. Whiting oversaw the production of the review, managed the review team and contributed to study selection and data extraction. Penny F. Whiting, Jenny L. Donovan and Theresa H.M. Moore drafted the manuscript. All authors contributed to and agreed the final draft. Penny F. Whiting, Theresa H.M. Moore and Jenny L. Donovan, are guarantors.

Conflicts of interest

None of the authors have any conflicts of interest to disclose. All authors had access to all the study data, take responsibility for the accuracy of the analysis, and had authority over manuscript preparation and the decision to submit the manuscript for publication. All authors approve the manuscript and agree to adhere to all terms outlined in Annals of Internal Medicine information for authors including terms for copyright.

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Abbreviations: ADT, androgen-deprivation therapy; AUASI, AUA Symptom Index; CES-D, Center for Epidemiologic Studies Depression scale; EMBASE, the Excerpta Medica database; EORTC QLQ-(C30)(PR25), European Organisation for Research and Treatment of Cancer quality of life questionnaire (30-item core) (prostate specific 25-item); EPIC, Expanded Prostate Cancer Index Composite; FACT(-G)(-P), Functional Assessment Of Cancer Therapy (General) (Prostate); ICS, International Continence Society; IIEF, International Index of Erectile Function; MAX-PC, Memorial Anxiety Scale for Prostate Cancer; NIHR, UK National Institute for Health Research; PROM, patient-reported outcome measure; QoL, quality of life; RCT, randomised controlled trial; RP, radical prostatectomy; SF(-12)(-36), short-form health survey (12-item) (36-item); SHIM, Sexual Health Inventory for Men; STAI-6, State-Trait Anxiety Inventory six-item; UCLA PCI, University of California, Los Angeles Prostate Cancer Index.

Supporting Information

Additional Supporting Information may be found in the online version of this article:

Appendix S1. EMBASE Search strategy.
Appendix S2. Study details.